



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/784,645	02/15/2001	Stephen A. Empedocles	019916-001210US	5563

20350 7590 05/09/2002

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER

FORMAN, BETTY J

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/09/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/784,645

Applicant(s)

EMPEDOCLES ET AL.

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 27-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 and 40-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Restrictions

1. Applicant's election without traverse of Group I, claims 1-26 and 40-43, filed 8 February 2002 in Paper No. 10 is acknowledged. Claims 27-39 are withdrawn from further consideration. Claims 1-26 and 40-43 are discussed below.

Information Disclosure Statement

2. The International Search Report and the references listed on the 1449 received 24 July 2001 have been reviewed and considered.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. Provisional Application 60/266,290 filed 29 September 2000 and 60/182,845 filed 16 February 2000 upon which priority is claimed provides adequate support under 35 U.S.C. 112 for claims 1-26 and 40-43 of this application.

Claim Objections

4. Claims 25, 40 and 42 are objected to because of the following informalities:
 - a. Claim 25 is objected to for the recitation "the antiligands is an aptamer" because the plural "antiligands" requires the plural verb "are".
 - b. Claims 40 is objected to in step (b) because "containing" appears to be missing after the recitation "or suspected of".

Art Unit: 1634

c. Claim 42 is objected to in line 3, because either "by" or "through" is incorrectly placed after "pair".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-26, 41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-26 are indefinite in Claim 1 because the claim is drawn to a method of detecting a ligand of interest, but the claims do not recite method steps of ligand detection. It is suggested that Claim 1 be amended to recite steps of ligand detection e.g. at the end of the claim insert "whereby the presence of the first semiconductor nanocrystal detects the presence of the ligand of interest".

b. Claims 3, 5, 7, 9 and 12 are indefinite in Claim 3 for the recitation "detectably distinct second semiconductor nanocrystal" because it is unclear how or within what relationship the second nanocrystal is distinct. It is suggested that Claim 3 be amended to clarify e.g. delete "detectably distinct" and after "nanocrystal" insert, "which is detectably distinct from the first semiconductor nanocrystal".

c. Claim 8 is indefinite for the recitation "the first ligand bears a single first semiconductor nanocrystal" because "bears" lacks proper antecedent basis in Claim 1 wherein the ligand is "linked". It is suggested that Claim 8 be amended to provide proper antecedent basis e.g. replace "bears" with "is linked to".

Art Unit: 1634

d. Claim 9 is indefinite for the recitation "the first ligand and the second ligand bear a single first and a single second semiconductor nanocrystal" because "bear" lacks proper antecedent basis in Claim 1 wherein the ligand is "linked". It is suggested that Claim 9 be amended to provide proper antecedent basis e.g. replace "bear" with "are linked to".

e. Claims 41 and 43 are indefinite in Claim 41 for recitation of the phrase "such that" because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 1-10, 13, 16-24 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Bawandi et al (U.S. Patent No. 6,306,610 B1, filed 17 September 1999).

Regarding Claim 1, Bawandi et al disclose a method of detecting a ligand comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distance locations to provide an array wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspecting of containing the first ligand wherein the first ligand is linked through a linker to a first semiconductor nanocrystal

Art Unit: 1634

after the contacting under conditions in which the first ligand binds specifically to the first anti-ligand to form a first complex; removing unbound ligand from the array; and identifying the location of the first complex by detecting the presence of the first complex of the first semiconductor nanocrystal (Column 22, lines 48-65 and Fig. 2).

Regarding Claim 2, Bawandi et al disclose the method wherein the linker comprises two members of a binding pair a first member attached to the first ligand and a second member attached to the first semiconductor (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 3, Bawandi et al disclose the method wherein the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to form a second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Regarding Claim 4, Bawandi et al disclose the method of Claim 1 wherein the anti-ligands are nucleic acid probes and the first ligand is a target nucleic acid (Column 5, line 18-26).

Regarding Claim 5, Bawandi et al disclose the method of Claim 3 wherein the anti-ligands are nucleic acid probes and the first ligand is a target nucleic acid (Column 5, line 18-26 and Column 26, lines 15-46).

Regarding Claim 6, Bawandi et al disclose the method comprising oligonucleotides (i.e. antiligands) immobilized onto an array and contacting the array with probes (i.e. ligands) wherein the probes are linked to the semiconductor nanocrystal prior to the contacting step (Column 26, lines 15-46, especially, lines 17-22 and 36-40).

Regarding Claim 7, Bawandi et al disclose the method comprising first and second oligonucleotides (i.e. antiligands) immobilized onto an array and contacting the array with

Art Unit: 1634

probes (i.e. ligands) wherein the probes are linked to the semiconductor nanocrystal prior to the contacting step (Column 26, lines 15-46, especially, lines 41-46 and multiplex assay).

Regarding Claim 8, Bawandi et al disclose the method wherein the first ligand bears a single first semiconductor nanocrystal (Column 26, lines 41-46).

Regarding Claim 9, Bawandi et al disclose the method wherein the first ligand and the second ligand bear a single first and second semiconductor nanocrystal (Column 26, lines 41-46).

Regarding Claim 10, Bawandi et al disclose the method wherein the linker comprises two members of a binding pair a first member attached to the first ligand and a second member attached to the first semiconductor (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 13, Bawandi et al disclose the method wherein the nucleic acid probes are allele-specific i.e. single nucleotide polymorphism (Column 20, lines 23-27)

Regarding Claim 16, Bawandi et al disclose the method wherein the plurality of anti-ligands are proteins (Column 5, lines 9-17).

Regarding Claim 17, Bawandi et al disclose the method wherein the ligand is a proteins (Column 5, lines 9-17).

Regarding Claim 18, Bawandi et al disclose the method wherein the anti-ligands are antibodies (Column 5, lines 9-17).

Regarding Claim 19, Bawandi et al disclose the method of Claim 16 wherein the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to form a second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Art Unit: 1634

Regarding Claim 20, Bawandi et al disclose the method wherein the anti-ligand is a component of a tissue specimen e.g. antibodies, proteins and nucleic acids (Column 5, lines 9-26).

Regarding Claim 21, Bawandi et al disclose the method of Claim 16 wherein the sample contains a second ligand linked to a detectably distinct second semiconductor nanocrystal, wherein the second ligand is capable of binding specifically to a second immobilized anti-ligand to form a second complex; and wherein identifying comprising determining which location of the array include the first complex, the second complex or first and second complex by detecting and quantifying the presence in the first and second complex i.e. multiplexing to detect antibody-specific antigens (Column 22, lines 59-67).

Regarding Claim 22, Bawandi et al disclose the method wherein the anti-ligand is selected from the group consisting of proteins and nucleic acid targets and the ligands are selected from the group consisting of antibodies and nucleic acid probes (Column 5, lines 9-26).

Regarding Claim 23, Bawandi et al disclose the method wherein the anti-ligands are distinct target nucleic acids and the ligands are nucleic acid probes (Column 8, lines 22-28).

Regarding Claim 24, Bawandi et al disclose the method wherein the anti-ligands are proteins and the ligands are proteins (Column 5, lines 9-17).

Regarding Claim 40, Bawandi et al disclose a method comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distinct locations thereon to provide a first array, wherein the plurality comprises a first anti-ligand that is a binding partner of a first ligand; contacting the first array with a sample containing or suspected of containing the first ligand whereby the first ligand and the first anti-ligand interact to form a first complex; labeling the first ligand in the first complex with a first semiconductor nanocrystal; and identifying with location of the array includes the first complex

Art Unit: 1634

by detecting the presence of therein of the first semiconductor nanocrystal (Column 22, lines 48-67).

Regarding Claim 41, Bawandi et al disclose the method wherein the first plurality of anti-ligands comprises a second anti-ligand that is a binding partner of a second ligand; the sample contains or is suspected of containing the second ligand such that the second ligand and the second anti-ligand form a second complex; labeling the second ligand in the second complex with a second semiconductor nanocrystal that is detectably distinct from the first semiconductor nanocrystal; and determining which location on the array include the first complex, the second complex or both by detecting the presence of the nanocrystals (Column 22, line 59-Column 23, line 7).

Regarding Claim 42, Bawandi et al disclose the method wherein the first ligand comprises a first member of a first binding pair and the semiconductor nanocrystal is linked to a second member of the first binding pair through a linker (Column 7, lines 8-18 and Claims 3-4).

Regarding Claim 43, Bawandi et al disclose the method wherein the second ligand comprises a first member of a second binding pair and the second semiconductor nanocrystal is linked to a second member of the second binding pair (Column 7, lines 8-18 and Claims 3-4).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole

Art Unit: 1634

would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 11, 12, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bawandi et al (U.S. Patent No. 6,306,610 B1, filed 17 September 1999) and Gold et al (WO 99/31275, published 24 June 1999).

Regarding Claim 11, Bawandi et al teach the method of Claim 4 comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distance locations to provide an array wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspecting of containing the first ligand wherein the first ligand is linked through a linker to a first semiconductor nanocrystal after the contacting under conditions in which the first ligand binds specifically to the first anti-ligand to form a first complex; removing unbound ligand from the array; and identifying the location of the first complex by detecting the presence of the first complex of the first semiconductor nanocrystal (Column 22, lines 48-65 and Fig. 2) but they do not teach a second plurality of anti-ligands are immobilized to provide a second array. However, second arrays (i.e. multiple arrays) were well known in the art at the time the claimed invention was made as taught by Gold et al. Specifically, Gold et al teach that a second plurality of anti-ligands are immobilized at positionally distinct locations (page 14, lines 16-18) wherein one array is contacted with a test sample and the second array is contacted with a control to thereby diagnose the presence

Art Unit: 1634

of a disease pattern (page 4, lines 13-15, Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Bawandi et al by adding the second array as taught by Gold et al to thereby facilitate detection and diagnosis of a disease state as taught by Gold et al (page 4, lines 13-15).

Regarding Claim 12, Bawandi et al teach the method of Claim 5 comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distinct locations to provide an array wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspected of containing the first ligand wherein the first ligand is linked through a linker to a first semiconductor nanocrystal after the contacting under conditions in which the first ligand binds specifically to the first anti-ligand to form a first complex; removing unbound ligand from the array; and identifying the location of the first complex by detecting the presence of the first complex of the first semiconductor nanocrystal (Column 22, lines 59-67 and Fig. 2) but they do not teach a second plurality of anti-ligands are immobilized to provide a second array. However, second arrays (i.e. multiple arrays) were well known in the art at the time the claimed invention was made as taught by Gold et al. Specifically, Gold et al teach that a second plurality of anti-ligands are immobilized at positionally distinct locations (page 14, lines 16-18) wherein one array is contacted with a test sample and the second array is contacted with a control to thereby diagnose the presence of a disease pattern (page 4, lines 13-15, Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Bawandi et al by adding the second array as taught by Gold et al to thereby facilitate detection and diagnosis of a disease state as taught by Gold et al (page 4, lines 13-15).

Regarding Claim 25, Bawandi et al teach the method of Claim 1 wherein the anti-ligands are nucleic acid-specific oligonucleotides (Column 5, lines 20-26) but they do not specifically teach the oligonucleotides are aptamers. However, aptamers were well known in the art at the time the claimed invention was made as taught by Gold et al. Specifically, Gold

Art Unit: 1634

et al teach that a similar method comprising immobilizing a plurality of anti-ligands at positionally distinct locations to form an array and contacting the array with a sample to identify ligands which bind the anti-ligands wherein the anti-ligands are aptamers (page 2, line 25-page 3, line 25) and they teach the aptamer identification facilitates disease diagnosis and/or prognosis (page 2, lines 25-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the aptamer anti-ligand teaching of Gold et al to the anti-ligand array of Bawandi et al and to immobilize aptamers to thereby detect aptamer-specific ligands by detecting the attached semiconductor nanocrystals. One skilled in the art would have been motivated to immobilize aptamers based on the clinical importance of aptamers taught by Gold et al (page 2, lines 25-30). The skilled practitioner would have been further motivated to label the anti-ligand-ligand complex with the semiconductor nanocrystals based on the nanocrystals high intensity, long-lasting and tunable signal as taught by Bawandi et al (Column 4, lines 40-54) to thereby detect the clinically important complexes efficiently and accurately in a multiplex format for the obvious benefits of qualitative and quantitative diagnostics.

Regarding Claim 26, Bawandi et al teach the method of Claim 1 wherein the ligands comprise any compound associated with biological functions e.g. nucleic acids (Column 5, lines 3-8) but they do not specifically teach the ligands are aptamers. However, aptamers were well known in the art at the time the claimed invention was made as taught by Gold et al. Specifically, Gold et al teach that a similar method comprising immobilizing a plurality of anti-ligands at positionally distinct locations to form an array and contacting the array with a sample to identify ligands which bind the anti-ligands wherein the ligands are aptamers (page 15, line 27-page 16, line 3) and they teach the aptamer identification facilitates disease diagnosis and/or prognosis (page 2, lines 25-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the aptamer anti-ligand teaching of Gold et al to the anti-ligand array of Bawandi et al and to immobilize

Art Unit: 1634

aptamer-specific anti-ligands to thereby detect aptamer complexes by detecting the attached semiconductor nanocrystals. One skilled in the art would have been motivated to immobilize aptamer-specific anti-ligands based on the clinical importance of aptamers taught by Gold et al (page 2, lines 25-30). The skilled practitioner would have been further motivated to label the anti-ligand-ligand complex with the semiconductor nanocrystals based on the high intensity, long-lasting and tunable signal provided by nanocrystals as taught by Bawandi et al (Column 4, lines 40-54) to thereby detect the clinically important complexes efficiently and accurately in a multiplex format for the obvious benefits of qualitative and quantitative diagnostics.

11. Claims 14 and 15 rejected under 35 U.S.C. 103(a) as being unpatentable over Bawandi et al (U.S. Patent No. 6,306,610 B1, filed 17 September 1999) and Koster et al (5,605,798, issued 25 February 1997).

Regarding Claim 14, Bawandi et al teach the method of Claim 4 comprising: providing a first plurality of anti-ligands immobilized on a solid support at positionally distance locations to provide an array wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspecting of containing the first ligand wherein the first ligand is linked through a linker to a first semiconductor nanocrystal after the contacting under conditions in which the first ligand binds specifically to the first anti-ligand to form a first complex; removing unbound ligand from the array; and identifying the location of the first complex by detecting the presence of the first complex of the first semiconductor nanocrystal (Column 22, lines 48-65 and Fig. 2) wherein the nucleic acid probes are allele-specific i.e. single nucleotide polymorphism (Column 20, lines 23-27) but they do not specifically teach the plurality of probes comprises a set of capture probes, each capable of forming a hybridization complex with a distinct allelic form of the target at the allelic site.

Art Unit: 1634

However, Koster et al teach a similar method comprising providing a first plurality of anti-ligands immobilized on a solid support wherein the anti-ligands are capable of binding specifically to a first ligand; contacting the array with a sample containing or suspecting of containing the first ligand to form a first complex wherein the nucleic acid probes are allele-specific and wherein the plurality of probes comprising a set of capture probes each capable of forming a hybridization complex with a distinct allelic form of the target at the allelic site (Column 11, lines 56-67). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the allele-specific probes and capture probes as taught by Koster et al to the target-specific array of Bawandi et al and to immobilize allele-specific anti-ligands to thereby detect allele-specific complexes by detecting the attached semiconductor nanocrystals. One skilled in the art would have been motivated to immobilize allele-specific anti-ligands based on the well known clinical importance of alleles as taught by Koster (Column 11, lines 19-24). The skilled practitioner would have been further motivated to label the allele-specific complex with the semiconductor nanocrystals based on the high intensity, long-lasting and tunable signal provided by nanocrystals as taught by Bawandi et al (Column 4, lines 40-54) to thereby detect the clinically important complexes efficiently and accurately in a multiplex format for the obvious benefits of qualitative and quantitative diagnostics.

Regarding Claim 15, Bawandi et al teach the method wherein the targets within the complexes are contacted with a pool of probes comprising the semiconductor nanocrystals (i.e. secondary antibodies Column 22, lines 54-58 and Fig. 2) wherein identifying comprises determining which of the detection probes is bound to the target (Column 22, lines 62-67) but they do not teach the probes are allele-specific detection probes. However, Koster et al teach the similar method wherein the detection probes are allele specific (Column 11, lines 56-67). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the allele-specific probes and capture probes as taught by Koster et al to the

Art Unit: 1634

target-specific array of Bawandi et al and to immobilize allele-specific anti-ligands to thereby detect allele-specific complexes by detecting the attached semiconductor nanocrystals. One skilled in the art would have been motivated to immobilize allele-specific anti-ligands based on the well known clinical importance of alleles as taught by Koster (Column 11, lines 19-24). The skilled practitioner would have been further motivated to label the allele-specific complex with the semiconductor nanocrystals based on the high intensity, long-lasting and tunable signal provided by nanocrystals as taught by Bawandi et al (Column 4, lines 40-54) to thereby detect the clinically important complexes efficiently and accurately in a multiplex format for the obvious benefits of qualitative and quantitative diagnostics.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-10, 16-26 and 40-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,274,323 B1 in view of Koster (U.S. Patent No. 5,606,789, issued 25 February 1997).

Although the conflicting claims are not identical, they are not patentably distinct from each

Art Unit: 1634

other because both sets of claims are drawn to methods for detecting a target molecule by detecting fluorescence emitted by a semiconductor nanocrystal and differ only in the patent claims being drawn to the a single species of target molecule (i.e. polynucleotide) a single species of affinity moiety (i.e. PCR product) various species of first and second binding members (e.g. avidin and streptavidin, digoxigenin and anti-digoxigenin) while the instant claims are drawn to the genus ligand, anti-ligand and first and second binding pairs. The courts have stated that a genus is obvious in view of the teaching of a species (see; *In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) and MPEP 2131.02). Therefore, the instantly claimed methods drawn to the genus target molecule and affinity moiety are obvious in view of the patent methods drawn to the species. The sets of claims differ also in the that instant claims are drawn to immobilized anti-ligand. However, immobilized anti-ligands were well known in the art at the time the claimed invention was made as taught by Koster who teach a similar method of detecting a target molecules wherein the anti-ligand is immobilized whereby detection of the anti-ligand is facilitated (Column 7, lines 19-29 and 54-56). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the patent detection by immobilizing the anti-ligand as instantly claimed because one of skill in the art would have been motivated to immobilized the anti-ligand to thereby facilitate target detection as taught by Koster (Column 7, lines 54-56).

14. Claims 1-10, 16-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 12-15 of copending Application No. 09/784,866. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods for detecting targets immobilized on a substrate using the same method steps i.e. by

Art Unit: 1634

detecting a semiconductor nanocrystal (quantum dot) and differ only in the instant claims being drawn to the drawn to the detecting a "ligand" while the '866 application is drawn to detecting a "target species". However, the instantly claimed "ligand" (Claims 4, 16-19 and 21) and the '866 "target species" (Claim 10) are both selected from the group consisting of nucleic acids, proteins, antibodies and aptamers. Therefore the sets of claims are essentially the same and differ only in the arrangement and grouping of the claim limitations. Hence, the instant claims are obvious in view of the '866 claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 1-10, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 17-22, 28-39 of copending Application No. 09/766,273. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations i.e. immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the '273 claims are drawn to a species of ligand and anti-ligand (i.e. polynucleotide) while the instant independent claims are broadly drawn to the genus ligand and anti-ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see *Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly

Art Unit: 1634

claimed ligand and anti-ligand (i.e. genus) is obvious in view of the '273, polynucleotide (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 1-10, 13-15, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 09/882,193. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations. Both sets of claims are drawn to method comprising the steps of immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the '193 claims are drawn to a species of ligand and anti-ligand (i.e. target nucleic acid and complementary primer) while the instant independent claims are broadly drawn to the genus ligand and anti-ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand and anti-ligand (i.e. genus) is obvious in view of the '193, target nucleic acid and complementary primer (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art Unit: 1634

17. Claims 1-10, 20-26 and 40-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25, 27-29, 32, 35-39 and 53 of copending Application No. 09/887,914. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations i.e. immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the '914 claims are drawn to a species of ligand (i.e. polymerase chain reaction product) while the instant independent claims are broadly drawn to the genus ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see *Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand (i.e. genus) is obvious in view of the '914, polymerase chain reaction product (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. No claim is allowed.

19. The examiner's Art Unit has changed from 1655 to 1634. Please address correspondence to Art Unit 1634.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

Application/Control Number: 09/784,645

Page 19

Art Unit: 1634

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
April 26, 2002